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Single Center Evaluation of Long-Term Results of Glargin U-300 in Insulin Naive Patients In a Real-World Setting

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ABSTRACT

Objective: Insulin therapy stands as one of the most effective and well-established therapeutic options for managing glycemic control in Diabetes Mellitus (DM). Glargine 300 U/mL (Gla-300) represents a new long-acting insulin analog, which has demonstrated a decrease in the risk of hypoglycemia and a reduction in the total number of injections due to prolonged insulin absorption. In this study, we investigated the long-term effects of Gla-300 on Fasting Plasma Glucose (FPG) and HbA1c levels, as well as the incidence of hypoglycemia in insulin-naive patients admitted to the Internal Medicine outpatient clinic, over a period of 0, 3, 6, 12, and 24 months..

Material and Methods: Between January 2018 and June 2022, insulin-naive patients diagnosed with Type 2 Diabetes Mellitus (T2DM) who initiated treatment with Gla-300 and sought care at the Internal Medicine outpatient clinic were subjected to retrospective analysis.

Results: The study included 49 insulin-naive patients. A statistically significant decrease was observed in Fasting Plasma Glucose (FPG) ($p = 0.03$) and HbA1c ($p = 0.02$) levels during the 24-month follow-up period of Glargine U-300. Additionally, a significant reduction in both FPG ($p < 0.01$) and HbA1c ($p < 0.01$) values was achieved at the time of diagnosis and at 3 months. Hypoglycemia was reported in only 1 patient (2%) during our study, indicating a very low hypoglycemia rate.

Conclusion: Diabetes mellitus (DM) poses a significant public health challenge, resulting in economic burden and diminished quality of life. Developed to address these challenges, Gla-300 serves as a long-acting basal insulin that effectively reduces the risk of hypoglycemia while offering targeted glycemic control, as evidenced by our study findings. In Turkey, there is a pressing need for multicenter, prospective real-world studies that incorporate parameters such as insulin dosage and weight monitoring.

Keywords: Glargine 300 U, Long acting Insulin, Diabetes Mellitus, Hypoglycemia

INTRODUCTION

Diabetes Mellitus (DM) represents a significant public health challenge with a rapidly increasing prevalence worldwide (1). The primary objective in managing DM is to achieve glycemic control, which serves as the cornerstone in preventing long-term macro and micro complications such as retinopathy, neuropathy, nephropathy, myocardial infarction, and stroke (2). Insulin therapy stands as one of the most effective and well-established therapeutic options for managing glycemic control. While basal and rapid-acting insulin therapy combinations are preferred for patients with Type 1 DM, insulin therapy is considered as a second-line treatment for patients with Type 2 DM who do not achieve adequate glycemic control with oral antidiabetic medications (3). Hypoglycemia, the most common adverse effect of insulin therapy, is a significant concern for patients, often leading to reduced insulin utilization (3,4). However, the development of long-acting basal insulins has contributed to a decrease in the risk of hypoglycemia, along with a reduction in the total number of injections due to prolonged insulin absorption (5,6). Glargine 300 U/mL (Gla-300) emerges as a novel long-acting insulin analog (7).

In this study, we examined the long-term effects of Gla-300 on Fasting Plasma Glucose (FPG) and HbA1c levels, as well as the incidence of hypoglycemia, in insulin-naive patients attending the Internal Medicine outpatient clinic at Mersin City Training and Research Hospital. Data was collected at intervals of 0, 3, 6, 12, and 24 months between January 2018 and June 2022.

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MATERIAL and METHODs

Patients diagnosed with Diabetes Mellitus (DM), aged >18 years, and admitted to the Internal Medicine outpatient clinic between January 2018 and June 2022 were screened. Among 1200 patients receiving Gla-300 for DM, those with type 1 DM, previous insulin therapy, or inadequate follow-up were excluded. A total of 49 insulin-naive patients were enrolled in the study. Data on age, sex, DM history, comorbidities, complications, medications, additional treatments post-Gla-300 initiation, and FPG and HbA1c values at diagnosis and at 3, 6, 12, and 24 months were retrospectively extracted from electronic medical records.

Statistical Analysis

Data were analyzed using SPSS 21.0 (IBM Corp., Armonk, NY, USA). Normal distribution of study variables was assessed using the Kolmogorov–Smirnov test. Numerical variables were expressed as mean ± SD (standard deviation), while categorical variables were presented as numbers and percentages. Paired samples t-test was used to compare means between two related groups, and ANOVA test was employed for repeated measurements involving three or more groups. Ethical approval for non-invasive clinical research was obtained from the Mersin University Ethics Committee (2022/602).

RESULTs

Between January 2018 and June 2022, a total of 1200 patients with DM receiving Gla-300 were identified. Patients with type 1 DM, previous insulin therapy, or those with no follow-up were excluded from the study, resulting in 49 insulin-naive patients being included. Among the participants, 28 (57.1%) were women and 21 (42.9%) were men, with a mean age of 56.2 ± 6.9 years. The most common comorbidity was hypertension, present in 18 patients (36.3%), and the most prevalent complication was neuropathy, observed in 19 patients (38.8%). Additionally, 11 patients (22.4%) had not received any previous therapy. Demographic characteristics of the patients are summarized in **Table 1**.

During the 24-month follow-up, hypoglycemia was observed in 1 patient (2.0%). In addition to Glargine U-300, 7 patients (14.3%) were administered insulin aspart, 5 (10.2%) received insulin glulisine, and 2 (4.1%) were treated with insulin lispro. Overall, 14 patients (28.6%) received rapid-acting insulin analogs during the follow-up period. The changes in FPG and HbA1c values over time are illustrated in **Figure 1**.

A statistically significant decrease was observed in FPG ($p = 0.03$) and HbA1c ($p = 0.02$) during the 24-month follow-up of Glargine U-300. Significant decreases were also noted in FPG ($p < 0.01$) and HbA1c ($p < 0.01$) values at the time of diagnosis and at 3 months. However, there were no significant changes in FPG ($p = 0.6$) and HbA1c ($p = 0.3$) values at 3 months and 6 months, nor in FPG ($p = 0.7$) and HbA1c ($p = 0.7$) values at 6 months and 12 months, or at 12 months and 24 months (FPG: $p = 0.6$, HbA1c: $p = 0.7$). Additionally, these values remained stable over time. The FPG and HbA1c levels of patients using Glargine U-300 are summarized in **Table 2**.

Tablo 1. Demographic data of the patients

Features	n (%)
Female	28 (57.1)
Age mean± SD	56.2 ± 6.9
Diabetes mellitusyears mean± SD	12.9 ± 6.9
Comorbidity	
Hypertension	18 (36.7)
Hyperlipidemia	2 (4.1)
Coronary Artery Disease	2 (4.1)
Ankylosing Spondylitis	1 (2.1)
Ulcerative Colitis	2 (4.1)
Multiple Diseases	11 (22.4)
No diseases	13 (26,5)
Complications	
Neuropathy	19 (38.8)
Neuropathy+Retinopathy	5 (10.2)
Diabetic Foot	3 (6.1)
Chronic Renal Failure	3 (6.1)
Coronary Artery Disease	2 (4.1)
Oral Anti Diabetic Drugs	
Biguanide	4 (8.2)
Biguanide +Sulfonylurea	11 (22.4)
Thiazolidinedione+ Biguanide	2 (4.1)
Thiazolidinedione+ Biguanide+Sulfonylurea	7 (14.3)
Thiazolidinedione+ Biguanide+DPP-4	9 (18.4)
Thiazolidinedione+ Biguanide +SGLT-2	3 (6.1)
DPP4+SGLT-2	2 (4.1)
No	11 (22.4)

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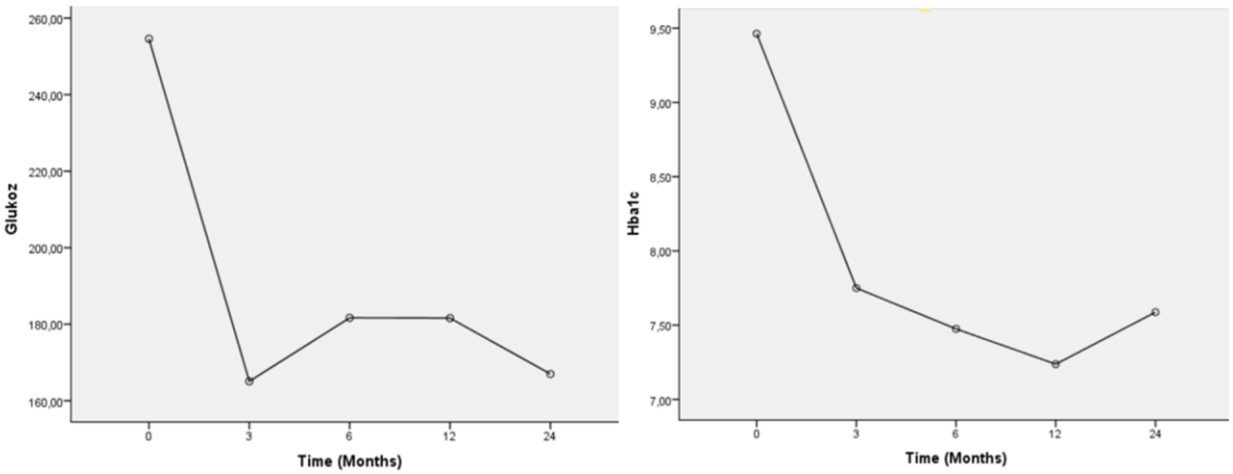

Figure 1. The change in Fast Plazma Glukoz and Hba1c values over time

Table 2. Fasting Plazma Glukoz and Hba1c levels in patients using Glargin U-300

Features	Months					*p*
	0	3	6	12	24	
Fasting Plazma Glucose mg/dl mean± SD	252±126.7	135.1±48,3	142.6±40.7	130.5±46.9	135.4±41.5	**0.03**
Hba1c mean± SD	9.4±1.9	7.8±1.5	7.5±0.9	7.2±1.3	7.5±1.2	**0.02**

DISCUSSION

The World Health Organization (WHO) has reported that type 2 diabetes mellitus (DM) is most prevalent in individuals aged 65 years or older in developed countries and in the middle-aged population in developing countries (8). In our study, the mean age was 56.2 ± 6.9 years, which aligns with the WHO data. While DM was traditionally assumed to be equally distributed between sexes, the NAHES-II study indicated that 55% of newly diagnosed DM cases are women (9,10), and it is predicted that DM will be 10% more common in women than men by 2025 (11). In our study, 57.1% of the patients were women, suggesting an increasing trend in women with DM.

Hypertension is observed 1.5–2 times more frequently in patients with diabetes mellitus (DM) compared to the general population and affects 30%–50% of individuals with Type 2 DM (12). Furthermore, neuropathy is the most common complication associated with DM (13). In our study, neuropathy emerged as the most prevalent complication with a frequency of 38.8%, while hypertension was identified as the most common comorbid condition at 36.3%, aligning with findings from the literature.

Cetinarslan et al. investigated 108 insulin-naive patients initiating insulin glargine U300 and found a statistically significant decrease in mean HbA1c levels from 9.4% at diagnosis to 7.5% and 7.3% at 12 and 24 weeks, respectively. Mean fasting plasma glucose (FPG) levels decreased from 194.7 mg/dl to 126.5 mg/dl at week 12 and 131 mg/dl at week 24 (14).

In a multicenter, prospective study, Galstyan et al. evaluated 4442 insulin-naive patients initiating insulin glargine U300. They reported HbA1c levels of 9.28 ± 1.0, 8.19 ± 1.04, 7.77 ± 1.06, and 7.38 ± 0.97 at 0, 3, 6, and 12 months, respectively (15). Another study showed an HbA1c level of 7 at 6 months (16).

In our study, HbA1c values were 9.4 ± 1.9, 7.8 ± 1.5, 7.5 ± 0.9, 7.2 ± 1.3, and 7.5 ± 1.2 at 0, 3, 6, 12, and 24 months, respectively, and targeted decreases in FPG were achieved during the 24-month follow-up.

As the risk of hypoglycemia associated with basal insulin therapies is low, they are considered cost-effective both in the short and long terms. Short-term health expenditures primarily result from a reduction in hypoglycemia symptoms (17). Decreased anxiety about experiencing hypoglycemia reduces the likelihood of treatment discontinuation, leading to fewer long-term complications of diabetes mellitus (DM). Consequently, improved patient comfort and a general reduction in health expenditures are achieved both in the short and long terms (18).

Galstyan et al. reported a hypoglycemia incidence of 1.99% with Gla-300 over a 12-month period (15), noting that their findings were consistent with other studies demonstrating low rates of hypoglycemia associated with Gla-300 use (19,20). In our study, hypoglycemia was observed in only 1 patient (2%), indicating a very low hypoglycemia rate similar to that reported in other studies. This suggests that Gla-300 is a cost-effective insulin analog.

The limitations of our study include the absence of pre- and post-treatment weight and insulin doses due to the retrospective design, as well as the inability to generalize the results to the broader population given the study's single-center cross-sectional nature and small sample size. However, our study's strength lies in being the first real-world investigation conducted in our region among insulin-naive patients, spanning a lengthy period of 24 months.

CONCLUSION

Diabetes mellitus (DM) represents a significant public health concern, contributing to economic burdens and diminished quality of life. In response, various therapeutic interventions are being developed to enhance quality of life and mitigate complications. Among these developments, Gla-300 has emerged as a long-acting basal insulin capable of reducing the risk of hypoglycemia while offering precise glycemic control, as evidenced by our study's findings. In Turkey, there is a pressing need for multicenter, prospective real-world studies incorporating parameters such as insulin dosage and weight monitoring.

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Conflict of interest: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author Contributions: DG, SME: Designed and directed the study, Literature search, Data collection, Statistics **DG, SME:** Article writing, Final revisions. All authors reviewed the results and approved the final version of the manuscript.

Ethical approval: The present study was conducted in strict accordance with the principles outlined in the Declaration of Helsinki. Ethical approval for the study was obtained from the appropriate ethics committee.

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